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Nwhator, S.O.

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## Born too young and likely to die; Should this continue?

Solomon O. Nwhator<sup>a,\*</sup>, Dirk-Rolf Gieselmann<sup>b</sup>, Anna-Maria Heikkinen<sup>c</sup>,  
Michael Lazzara<sup>b</sup>, Taina Tervahartia<sup>c</sup>, Timo Sorsa<sup>c,d</sup>

<sup>a</sup> Department of Oral and Maxillofacial Diseases & Doctoral program in Oral Sciences, Faculty of Medicine, University of Helsinki, Finland

<sup>b</sup> Institute for Molecular Diagnostics, 42697 Solingen, Germany

<sup>c</sup> Department of Oral and Maxillofacial Diseases, University of Helsinki, Helsinki University Central Hospital, 00014 Helsinki, Finland

<sup>d</sup> Division of Periodontology, Department of Dental Medicine, Karolinska Institutet, 17177 Stockholm, Sweden



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### Introduction

Preterm birth can be easily described as a black man's problem with strong evidence to support the seemingly sweeping claim. Since 2016, there has been a yearly increase in the prevalence of preterm births among non-Hispanic blacks as released by the National Center for Health Statistics of the United States in 2018 [1]. Some of the children survive the immediate problems surrounding being born preterm, but this does not guarantee a healthy life thereafter. "Her baby was 7 weeks premature, and is fighting pneumonia. If Lerma departs, the hospital will no longer pay for the medication" [2]. But, the sufferings of children like Lerma's are life-long because survivors of preterm birth have an increased risk of long-term memory deficits and associated hippocampal alterations" [3]. These scenarios are familiar among non-Hispanic black women who are twice as likely to experience preterm birth [4] compared with women of the non-Hispanic white race; but should this continue? The rise of current global trends of disturbing racial disparity of preterm birth should not continue, especially with a little light shining in the dark; the light of a possible panacea! This possible panacea was announced by Helsinki researchers who stumbled upon the possible missing link in the racial disparity in preterm birth as reported in June 2018 [5].

The conclusion came after a series of studies with interesting findings which could hold the key to unraveling global racial disparities in preterm birth. The objectives of the studies were to assess the validity, sensitivity and specificity of a rapid aMMP-8 chairside test in the detection and prediction of periodontitis among Africans and Caucasians and to investigate how chronic periodontitis measured by this chairside test affects time to conception. The active Matrix Metalloproteinase-8 was chosen based on evidence from years of study and its several important characteristics including destruction of all components of the ECM & basement membrane and regulation of many processes, including inflammation [6]. MMP-8 is the most abundant MMP produced by the gingivae [7] and the levels of the active form (aMMP-8) correlate with severity of gum disease making it therefore the best predictor of periodontal inflammation, increasing with periodontal inflammation and reducing with periodontal treatment [7–9].

\* Corresponding author.

E-mail address: [solomon.nwhator@helsinki.fi](mailto:solomon.nwhator@helsinki.fi) (S.O. Nwhator).

**Table 1**  
aMMP-8 test results by number of periodontal pockets & Bleeding On Probing (BOP).

Number	Immunoassay positive	Immunoassay negative	Total	p-value
≥ 2 pockets	18	1	19	
< 2 pockets	34	23	57	
Total	52	24	76	0.003
≥ 2 sites with BOP	19	4	23	0.000
	6	15	21	
Total	25	19	44	

The table shows a strong association between the chairside test and two or more periodontal pockets ( $p = 0.003$ ) and BOP ( $p = 0.000$ ).

**Table 2**  
aMMP-8 chairside test results by age group & trimester of pregnancy.

	aMMP-8 level				p-value
	Normal		Elevated		
	n	%	n	%	
20–25 years	2	11.8	15	88.2	0.93
26–31 years	9	13.8	56	86.2	
> 31 years	6	11.5	46	88.5	
Total	17	12.7	117	87.3	
1st trimester	4	15.4	22	84.6	
2nd trimester	10	13.2	66	86.8	0.62
3rd trimester	3	9.4	29	90.6	
Total	17	12.7	117	87.3	



**Fig. 1.** Lateral immuno-assay kit. Two lines as shown indicate elevated aMMP-8 level. (A single blue line serves as control, indicating that the test is valid). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

## Main findings

The study participants included systemically healthy women who were either pregnant or fertility clinic attendees with the exception of women on fertility medications as well as those who got pregnant through fertility medications. Women who were not trying to get pregnant or with a history of not having regular sexual intercourse were excluded from the study. Smokers were also excluded from the study except a single woman who was found to be a smoker. Based on the inclusion criteria, 70 pregnant women and 58 fertility clinic attendees were included in the studies. From our studies, the chairside a-MMP-8 test was 82.6% sensitive for bleeding on probing, 95% sensitive for periodontitis and 96% sensitive for poor oral hygiene among adults. The test was also 76.5% sensitive for initial periodontitis and 71.8% sensitive for bleeding on probing among adolescents emanating from strong correlations with two sites with periodontal pockets. (Table 1) We also found widespread (87.3%) elevation of aMMP-8 among black pregnant Nigerians across all age groups and trimesters (Table 2). Also, the odds of increased conception were higher with the aMMP-8 chairside test-assessed periodontitis risk (OR 0.157, 95% CI 0.041–0.600  $P < 0.01$ ) all using a simple test based on aMMP-8 (Fig. 1).

The table shows that 87.3% of the pregnant women had elevated aMMP-8 levels across all agegroups and trimesters with no statistical differences by age group ( $p = 0.93$ ) and trimester ( $p = 0.62$ ).

## Discussion

Our findings are at extreme variance with the report on a Caucasian cohort of pregnant women, among which aMMP-8 levels actually reduced during pregnancy [10]. The etiology of preterm birth and its racial disparity is a global concern. Several hypotheses have emanated in an attempt to explain this racial disparity. It is interesting to note that despite the several hypotheses in the literature, researchers have only concluded that racial disparities in preterm birth remain poorly understood. The fact that close to 90 per cent of the black women had elevated aMMP-8 cannot be overlooked. Could our findings explain the high prevalence of preterm birth among black women compared with Caucasians? While the findings from our study are too early to make conclusions, the explanation of a possible link between aMMP-8 and the preponderance of preterm birth is indeed plausible since aMMP-8 levels closely correlate with the severity of periodontitis. More so,

aMMP-8 is the most abundant metalloproteinase produced by gingival and periodontal tissues [7]. We already know that periodontitis enhances endotoxemia and elevated aMMP-8 and low-grade systemic inflammation. This low-grade inflammation and its attendant effect at distant sites imply that the periodontium acts like an endocrine organ [11].

Interestingly, we detected this potentially-ground-breaking results using a simple test to quantitatively measure aMMP-8 levels in black pregnant women. The reader (image available at <https://www.alf-reader.com/>) is useful even where there is no dentist and could save many lives [12]. Now, it is well-known that preterm birth is closely associated with the activation of the metalloproteinases and is 'an early event in premature labor [SIC] and premature rupture of membranes' [12]. Lots of arguments of the multifaceted nature of the etiology of preterm labor have been put forward. Do these arguments foreclose the plausibility of selective predisposition of black women to preterm birth as a result of differential metalloproteinase levels. One of these angles is the genetic angle which could be explored in an attempt to explain why black women are more predisposed to pre-term birth. This angle enjoys biologic plausibility because LPS levels positively correlate with infection a position further supported by the greater prevalence of amniotic fluid markers of inflammation further supports this view [13,14]. The infections angle enjoys even more support by reports of elevated matrix metalloproteinases among women suffering from bacterial vaginosis [15]. Fiscella even declared that 'significantly higher rates of bacterial vaginosis among black women may account for nearly 30% of the racial gap in preterm births' Unfortunately, Adesiji and colleagues found no such association between bacterial vaginosis and preterm birth among Nigerian women [16]. The closest association was reported between malaria and preterm birth (Omole-Ohonsi & Attah, 2012). Surprisingly, the role of metalloproteinases in parasitic infections like malaria have been associated with elevated MMPs including MMP-8 [17]. Clearly therefore, the impact of elevated MMPs especially aMMP-8 found in about 90% of pregnant Nigerian women can neither be taken lightly, nor wished away. What if we investigated further, what if we could save just one child through this simple chairside test? [18] This is cheaper than the attendant life-long deficits experienced by babies born too young and would definitely be a great step towards improving young lives!

## Conclusion

The near total elevation of aMMP-8 levels among black women as discovered in our studies is worth further investigation. This might hold an important missing link in the thought-provoking racial disparity of preterm birth. We do not claim to have found the reason for the racial disparity in preterm birth, but we have definitely found something worth further investigation.

The full PhD dissertation can be assessed freely online at <http://urn.fi/URN:ISBN:978-951-51-4058-6>. (URN:ISBN:978-951-51-4058-6)

## Conflict of interest

The authors declare no conflicts of interest. Timo Sorsa is a co-inventor of patents (US-patent numbers 5652223, 5736341, 5866432, 6143476) on the use of MMPs and their inhibitors for diagnostic purposes.

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